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PATENT

Attorney Docket No. A-68990-3/RFT/RMS/RMK

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Dahiyat, *et al.*

Serial No. 09/981,289

Filed: October 15, 2001

For: *Design and Discovery of Protein Based TNF-a Variants for the Treatment of TNF-a Related Disorders*

Group No. 1647

Examiner: Seharaseyon, Jegatheesan

CERTIFICATE OF MAILING

I hereby certify that this correspondence, including listed enclosures, are being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231 on:

Date: February 4, 2003

Signature _____

Mary McFarland

DECLARATION UNDER 37 C.F.R. § 1.132 and M.P.E.P. § 716.09

Assistant Commissioner of Patents
Washington, DC 20231

Sir:

I, Robert J. Hayes, do hereby declare as follows:

1. I received a Ph.D. degree in Biochemistry and Molecular Biology in 1988 from the Imperial College of Science, London University.

2. Attached to this Declaration as Exhibit A are a copy of my curriculum vitae and a list of publications.

3. I have been employed at Xencor, the assignee of the above-identified application since 1998, first as a lead scientist, as the Director of Molecular Biology, and now as the Director of Antibody Technology.

4. One of my responsibilities at Xencor was to express and characterize Protein Design Automation® (PDA™) redesigned proteins.

5. I have read and I understand the above-identified patent application, and the Office Action mailed October 22, 2002.

6. Based on my understanding, the present invention describes computational methods for the design of protein variants or non-naturally occurring proteins.

7. The Examiner's main point appears to be that the novel proteins generated by computational modeling described in the present invention are unpredictable and insufficient to ensure the biological activity of a variant protein produced using the methods of the present invention. I disagree for the following reasons.

8. To the best of my recollection, all of the PDA™ technology redesigned proteins that I have expressed and characterized were functional for the biological property being tested.

9. Specific examples of the proteins that I have expressed and characterized are listed below:

a) granulocyte-colony stimulating factor PDA™ technology redesigned variants described by Luo at et al. (attached hereto as Exhibit B) and in U.S.S.N. 09/470,313 (attached hereto as Exhibit C);

b) human growth hormone variants PDA™ technology redesigned variants described by Filikov et al., (Protein Science, 11:1452-1461 (2002); attached hereto as Exhibit D) and U.S.S.N. 09/571,024, (attached hereto as Exhibit E); and,

c) xylanase PDA™ technology redesigned variants described in U.S.S.N. 09/570,856 (attached hereto as Exhibit F).

13. It is my belief that the PDA™ technology method described in the present invention is predictable and sufficient to ensure variant proteins with desired functional properties.

14. Finally, in my opinion the PDA™ technology redesigned protein variants of the present invention are sufficiently described to allow one of skill in the art to obtain functional proteins without undue experimentation.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful, false statements may jeopardize the validity/enforceability of the application or any patent issued thereon.

Date: 2/3/2003

Robert J. Hayes, Ph.D.